

<400> SEQUENCE: 8

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What is claimed is:

1. A composition comprising an interfering RNA that silences SMAD4 gene expression, wherein the interfering RNA is an siRNA that comprises a sense strand and a complementary antisense strand, wherein the siRNA is Identifier 3 (SEQ ID NO:7 and SEQ ID NO:8).

2. The composition of claim 1, further comprising a pharmaceutically acceptable carrier.

3. A nucleic acid-lipid particle comprising:

(a) an interfering RNA that silences SMAD4 gene expression, wherein the interfering RNA is an siRNA that comprises a sense strand and a complementary antisense strand, wherein the siRNA is Identifier 3 (SEQ ID NO:7 and SEQ ID NO:8);

(b) a cationic lipid; and

(c) a non-cationic lipid.

4. The nucleic acid-lipid particle of claim 3, wherein the cationic lipid comprises 1,2-dilinoleyloxy-N,N-dimethylaminopropane (DLinDMA), 1,2-dilinolenyloxy-N,N-dimethylaminopropane (DLenDMA), 1,2-di-y-linolenyloxy-N,N-dimethylaminopropane (y-DLenDMA), a salt thereof, or a mixture thereof.

5. The nucleic acid-lipid particle of claim 3, wherein the cationic lipid comprises 2,2-dilinoleyl-4-(2-dimethylaminoethyl)-[1,3]-dioxolane (DLin-K-C2-DMA), 2,2-dilinoleyl-4-dimethylaminomethyl-1,3]-dioxolane (DLin-K-DMA), a salt thereof, or a mixture thereof.

6. The nucleic acid-lipid particle of claim 3, wherein the cationic lipid comprises (6Z,9Z,28Z,31Z)-heptatriaconta-6,9,28,31-tetraen-19-yl 4-(dimethylamino) butanoate (DLin-M-C3-DMA), dilinoleylmethyl-3-dimethylaminopropionate (DLin-MC2-DMA), a salt thereof, or a mixture thereof.

7. The nucleic acid-lipid particle of claim 6, wherein the cationic lipid is DLin-M-C3-DMA, a salt thereof.

8. The nucleic acid-lipid particle of claim 3, wherein the non-cationic lipid is a phospholipid.

9. The nucleic acid-lipid particle of claim 3, wherein the non-cationic lipid is cholesterol or a derivative thereof.

10. The nucleic acid-lipid particle of claim 9, wherein the non-cationic lipid is cholesterol.

11. The nucleic acid-lipid particle of claim 3, wherein the non-cationic lipid is a mixture of a phospholipid and cholesterol or a derivative thereof.

12. The nucleic acid-lipid particle of claim 3, wherein the phospholipid comprises dipalmitoylphosphatidylcholine (DPPC), distearoylphosphatidylcholine (DSPC), or a mixture thereof.

13. The nucleic acid-lipid particle of claim 3, wherein the non-cationic lipid is a mixture of DPPC and cholesterol.

14. The nucleic acid-lipid particle of claim 3, further comprising a conjugated lipid that inhibits aggregation of particles.

15. The nucleic acid-lipid particle of claim 14, wherein the conjugated lipid that inhibits aggregation of particles is a polyethyleneglycol (PEG)-lipid conjugate.

16. The nucleic acid-lipid particle of claim 15, wherein the PEG-lipid conjugate is selected from the group consisting of a PEG-diacylglycerol (PEG-DAG) conjugate, a PEG-dialky-

loxypropyl (PEG-DAA) conjugate, a PEG-phospholipid conjugate, a PEGceramide (PEG-Cer) conjugate, and a mixture thereof.

17. The nucleic acid-lipid particle of claim 15, wherein the PEG-lipid conjugate is a PEG-DAA conjugate.

18. The nucleic acid-lipid particle of claim 17, wherein the PEG-DAA conjugate is selected from the group consisting of a PEG-didecyloxypropyl (C10) conjugate, a PEG-dilauryloxypropyl (C12) conjugate, a PEG-dimyristyloxypropyl (C14) conjugate, a PEG-dipalmitoyloxypropyl (C16) conjugate, a PEG-distearoyloxypropyl (C18) conjugate, and a mixture thereof.

19. The nucleic acid-lipid particle of claim 14, wherein the conjugated lipid that inhibits aggregation of particles is a polyoxazoline (POZ)-lipid conjugate.

20. The nucleic acid-lipid particle of claim 19, wherein the POZ-lipid conjugate is a POZ-DAA conjugate.

21. The nucleic acid-lipid particle of claim 14, wherein the cationic lipid is (6Z,9Z,28Z,31Z)-heptatriaconta-6,9,28,31-tetraen-19-yl 4-(dimethylamino) butanoate (DLin-M-C3-DMA), the non-cationic lipid is cholesterol, and the conjugated lipid is a polyethyleneglycol (PEG)-lipid conjugate.

22. The nucleic acid-lipid particle of claim 3, wherein the interfering RNA is fully encapsulated in the particle.

23. The nucleic acid-lipid particle of claim 3, wherein the particle has a lipid:interfering RNA mass ratio of from about 5:1 to about 15:1.

24. The nucleic acid-lipid particle of claim 3, wherein the particle has a median diameter of from about 30 nm to about 150 nm.

25. The nucleic acid-lipid particle of claim 3, wherein the cationic lipid comprises from about 50 mol % to about 65 mol % of the total lipid present in the particle.

26. The nucleic acid-lipid particle of claim 3, wherein the non-cationic lipid comprises a mixture of a phospholipid and cholesterol or a derivative thereof, wherein the phospholipid comprises from about 4 mol % to about 10 mol % of the total lipid present in the particle and the cholesterol or derivative thereof comprises from about 30 mol % to about 40 mol % of the total lipid present in the particle.

27. The nucleic acid-lipid particle of claim 26, wherein the phospholipid comprises from about 5 mol % to about 9 mol % of the total lipid present in the particle and the cholesterol or derivative thereof comprises from about 32 mol % to about 37 mol % of the total lipid present in the particle.

28. The nucleic acid-lipid particle of claim 14, wherein the conjugated lipid that inhibits aggregation of particles comprises from about 0.5 mol % to about 2 mol % of the total lipid present in the particle.

29. A pharmaceutical composition comprising a nucleic acid-lipid particle of claim 3 and a pharmaceutically acceptable carrier.

30. A method for introducing an interfering RNA that silences SMAD4 gene expression into a cell, the method comprising:

(a) contacting the cell with a nucleic acid-lipid particle of claim 3.

31. The method of claim 30, wherein the cell is in a mammal.